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EXAMINER	
BALLARD, KIMBERLY	

ART UNIT	PAPER NUMBER
1649	

NOTIFICATION DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PATDOCTC@fr.com

Office Action Summary	Application No.	Applicant(s)	
	10/681,018	FALLON, JOAN M.	
	Examiner	Art Unit	
	Kimberly Ballard	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 October 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *51 and 53-171* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *See Continuation Sheet* is/are rejected.

7)☒ Claim(s) *63,76,78-80,91,104,106-108,118,130,132-134,155,167,170 and 171* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continuation of Disposition of Claims: Claims rejected are 51,53-62,64-75,77,81-90,92-103,105,109-117,119-129,131,135-154,156-166,168 and 169.

DETAILED ACTION

Formal Matters

1. Claims 51 and 57 have been amended, claim 52 has been cancelled, and new claims 58-171 have been added in the amendment filed October 28, 2009. Following the amendment, claims **51** and **53-171** are pending and under examination in the present office action.

2. The Examiner of your application in the USPTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Kimberly Ballard, Art Unit 1649.

Continued Examination Under 37 CFR 1.114

3. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on October 28, 2009 has been entered.

Withdrawn Objections and Claim Rejections

4. All objections and rejections of record of claim 52 are rendered moot as the applicant has canceled the claim.

5. The objection to claim 51, as encompassing non-elected subject matter, is withdrawn in view of Applicant's amendment to the claim.

6. The rejection of claims 51 and 53-57 under U.S.C 112, second paragraph, as being indefinite, is withdrawn in view of Applicant's amendments to the claims.

Maintained and New Claim Rejections

Claim Objections

7. Claims 51, 82, 109 and 135 are objected to because of the following informalities: the word "Autism" is capitalized in each of these claims. Although autism is a specific disease condition, it does not require capitalization as such. Appropriate correction is required.

Claims 76, 104, 130 and 167 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim should refer to other claims in the alternative only. See MPEP § 608.01(n). Accordingly, the claims have not been further treated on the merits.

Double Patenting

7. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory

obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

8. Claims 51, 53-61, 66, 75, 81-89, 93, 97-98, 103, 109-116, 120, 123-124, 129, 135-141, 148-153, 157, 160-161, and 166 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-14 of U.S. Patent No. 6,632,429 in view of Beck et al. (US 6,020,310, provided by applicants) and Bode et al. (*Clin Biochem.* 1986;19:333-37; of record). The rejection of claims 51 and 53-57 is maintained and is further applied to new claims 58-61, 66, 75, 81-89, 93, 97-98, 103, 109-116, 120, 123-124, 129, 135-141, 148-153, 157, 160-161, and 166. Note that the Bode reference was added as necessitated by newly added claim limitations. Although the conflicting claims are not identical, they are not patentably distinct from each other for the following reasons.

The present claims 51 and 53-57 drawn to a method for treating autism with digestive enzymes, wherein the method comprising administering CARS test; determining lowered fecal chymotrypsin level; and administering digestive enzymes.

Claims 1-7 of the patent are directed to the similar method except that they do not recite administering CARS test. However, before-, during, and after-treatment evaluation of a medical condition being treated such as autism is obvious as such is notoriously known and widely practiced in the field. For example, Beck teaches behavior evaluation of the autistic patients prior and post secretin treatment, and indicates that a more specific measure directly related to autism is the Childhood Autism Rating Scale (CARS) (the paragraph bridging columns 10 and 11). Therefore, it would be obvious to administer CARS test before the treatment to set up a reference line for determining the efficacy of the treatment later.

Moreover, it would also be obvious to determine fecal chymotrysin levels following treatment with the digestive enzymes to monitor/evaluate treatment efficacy. Additionally, it would have been obvious to measure the chymotrysin levels at 30°C using an enzyme spectrophotometry method, because Bode et al. demonstrate an idenitical method for photometric measurement of chymotrypsin levels in stool samples at 25°C. Determination of chymotrysin levels at 30°C instead of 25°C is clearly a result effective protocol parameter that would be subject to optimization by one of ordinary skill in the art. As such, the conflicting claims are not patentably distinct from each other.

In the response filed October 28, 2009, Applicant requests that the Examiner hold the double patenting rejection in abeyance pending a finding of allowability of one or more of the pending claims. Accordingly, the double patenting rejection of claims 51, 53-61, 66,

75, 81-89, 93, 97-98, 103, 109-116, 120, 123-124, 129, 135-141, 148-153, 157, 160-161, and 166 is maintained until such time as allowable subject matter is identified.

9. Claims 135, 142-147, 150, 151, 153, 154, 162-164 and 169 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-3, 5-13, and 21-35 of copending Application No. 12/283,090 (hereinafter the '090 application). Although the conflicting claims are not identical, they are not patentably distinct from each other because in each case the claims recite a method for treating an individual having autism comprising administering an effective amount of digestive enzymes. For example, the '090 application contains claims reciting that the method ameliorates one or more symptoms of the autistic disorder, including making eye contact, improved social interaction, reduced arm flapping, reduce hyperactivity, improved formed bowel movement, and improved toilet training (claims 2-8), which renders obvious present claim 153. Claims 31-35 of the '090 application also recite that the autistic individual suffers from gastrointestinal dysfunction, which addresses instant claim 154. Additionally, the claims of the '090 application recite that the digestive enzymes include lipase, amylase, protease, cellulase, sucrase and maltase (claim 10), a pancreatic enzyme (claim 13), or chymotrypsin or trypsin (claims 22-23), which addresses instant claims 142-147 and 162-164. Finally, the claims of the '090 application recite dosage and frequency of dosage limitations (claims 9, 11 and 12) that render obvious such limitations of present claims 150, 151 and 169.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

11. Claims 51, 53-62, 64-75, 77, 81-90, 92-103, 105, 109-117, 119-129, 131, 135-154, 156-166 and 168 are rejected under 35 U.S.C. 103(a) as being unpatentable over Beck et al. (US 6,020,310, provided by applicants), and in view of Bode et al. (*Clin Biochem* 1986; 19:333-37), and Sipos (US 4,079,125). The rejection of claims 51 and 53-57 is maintained for reasons of record and is further applied to new claims 58-62, 64-75, 77, 81-90, 92-103, 105, 109-117, 119-131, 135-154, 156-166 and 168 as set forth below.

Beck discloses that there are two subgroups of autistic patients, distinguished on the basis of gastrointestinal symptoms, blood secretin levels, the increase in serotonin level after secretin injection and the quantity and quality of fluid produced for secretin stimulation. Beck notes that a significant portion of patients with autistic behavior also suffer from gastrointestinal symptoms (column 3, lines 37-39). For example, there is high prevalence of other gastrointestinal abnormalities including inflammation in the esophagus and *digestive enzyme deficiencies* in children with autistic behavior, which supports a relationship between the presence of gastrointestinal dysfunctions and autism (column 4, lines 56-65). Beck observed that in a group of autistic children with chronic diarrhea, secretin administration caused an extraordinary increase in the production of pancreatic fluid secretion, and that these children showed impressive progress in their social, behavioral and language skills in follow-up clinical visits (column 4, lines 39-48). Therefore, Beck teaches a method of treating of a patient exhibiting autism comprising stimulating pancreatico-biliary fluid secretion by administration of secretin hormone (column 5, lines 39-43).

Further, Beck indicates that patients with chronic, non-infectious diarrhea with unclear etiology were analyzed by the full upper GI work-up including biopsies for histology measurement of the digestive enzymes of the small intestine and the pancreas (including chymotrypsin) (column 10, lines 12-17, and 36-40). Beck notes, for example, that digestive enzymes of the small intestine include lactase, maltase, sucrase and glucoamylase, and pancreatic enzymes include amylase, lipase, trypsin and chymotrysin (column 10, lines 16-17). For instance, the assessment of various

pancreatic digestive enzymes following secretin administration was performed in order to evaluate the efficacy of secretin infusion (column 16 and Table 8).

Additionally, Beck teaches behavioral evaluation of the autistic patients prior to and following secretin treatment, and indicates that a more specific measure directly related to autism is the Childhood Autism Rating Scale (CARS) (the paragraph bridging columns 10 and 11). For example, in one case study, three weeks following secretin administration the subject was reported to have significant improvements, including resolution of chronic diarrhea, increased toilet training, and improvements in eye contact, alertness, expressive language, and fine motor skills. The subject was again assessed at eight months, wherein he received a second secretin infusion (paragraph spanning columns 11-12). In another case study, the subject was observed to have improvements in cognitive skills following a single dosage of secretin, wherein assessment was made over a five week period. A second dose of secretin was given at 3 months, and again further improvements in social behavior were observed (column 12, lines 47-67). These individual results were noted to be consistent with group results.

In summary, Beck discloses a method for treating autistic individuals, particularly those exhibiting gastrointestinal problems, comprising administering one or more doses of secretin, wherein the secretin administration causes the release of pancreatic digestive enzymes and results in improvements in various autistic symptoms. Beck further teaches behavioral assessment of autistic symptoms as well as measurement of pancreatic digestive enzymes prior to and following secretin administration.

However, Beck does not explicitly teach the assessment fecal chymotrypsin levels as a means to determine the degree of autism in an individual prior to and following the administration of digestive enzymes to the individual, nor does Beck disclose using a particular level of chymotrypsin (a level less than the normal fecal chymotrypsin level), such as for an index for determining whether or not to administer the digestive enzymes.

Bode teaches a simple photometric determination of chymotrypsin activity in stool samples, which is for detection of exocrine pancreatic insufficiency, and that the method is easy to perform, inexpensive and does not place any undue stress on the patient (abstract, and the 1st paragraph of the left column, for example). Additionally, Bode teaches that normal chymotrypsin activity is >10 U/g (page 333, 2nd column, 1.2), wherein the normal range of chymotrypsin is 10 to 59.5 U/g and a pathological value is indicated to be 4.2 U/g (with a range of 0.6-8.2 U/g) (p. 334, 2.2). Bode also teaches that measurement of chymotrypsin levels was performed at 25°C (p. 335, 2.5). Further, Bode discloses that this highly sensitive technique can be used not only to diagnose pancreatic insufficiency, but also to therapeutically monitor patients having chronic pancreatitis of various degrees of severity (p. 336, paragraph spanning columns 1-2).

Sipos teaches enzyme compositions for ingestion by a mammal having a digestive disorder which is caused by an enzyme deficiency and which can be alleviated by enzyme supplements (column 1, lines 13-16). In particular, Sipos teaches digestive enzyme-containing compositions, which are capable of withstanding hours of exposure to gastric fluids while protecting the biological activity of the enzymes (abstract), and

that the principal active agents in the composition are enzymes including such pancreatic enzymes as amylase, lipase, cellulase, and protease, such as trypsin and chymotrypsin, among others (column 5, lines 20-39). Further, Sipos teaches that the total amount of the composition required to be administered to an enzyme-deficient patient will vary with the severity of the condition and the amount of food ingested, and the compositions is administered with each meal (column 9, lines 10-16).

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to modify the therapeutic method taught by Beck for treating autistic patients by administering digestive enzymes as taught by Sipos instead of secretin and also to evaluate the efficacy of treatment by assessing both pancreatic digestive enzyme function and the therapeutic effect on autistic symptoms prior to and following treatment. Testing of pancreatic enzyme levels and assessment of autistic symptoms performed prior to treatment would serve to establish a baseline for the individual being treated, which could then be used to monitor treatment efficacy and adjust future therapy accordingly. Based on the teachings of Bode, the skilled artisan would have recognized a convenient, non-invasive means for measuring at least one of the pancreatic digestive enzymes, chymotrypsin, which comprises spectrophotometric measurement of chymotrypsin in fecal samples. Based also on Bode's teachings and those of Sipos, one of ordinary skill in the art would have recognized that patients having a lowered (i.e., pathological) level of fecal chymotrypsin, which is indicative of a pancreatic insufficiency (i.e., a digestive enzyme insufficiency), would stand to benefit from supplementation with digestive enzymes. Administration of Sipos' orally-

administered digestive enzymes would be an attractive alternative to secretin infusion, as it is less invasive and would therefore be easier to administer, particularly to young autistic patients. The person of ordinary skill in the art would have been motivated to do so for disease treatment, and would reasonably have expected success because Beck has demonstrated that autistic patients with digestive enzyme deficiencies can be treated when pancreatic fluid secretion is increased, and Sipos has demonstrated that the digestive enzyme-containing compositions are capable of withstanding hours of exposure to gastric fluids while still remaining biologically active.

With respect to the limitation regarding the administration of a CARS (childhood autism rating scale) test prior to and following administration of digestive enzymes to determine the degree in which autism symptoms are present, as in claims 51, 59-61, 64, 81, 82, 89, 109, 116, 136-138, and 153, pre-, during, and post-treatment evaluation of a medical condition being treated is obvious as such is notoriously known and widely practiced in the field. For example, Beck teaches behavior evaluation of the autistic symptoms in patients prior to and post-secretin treatment, wherein assessment included evaluation of the same types of behavioral symptoms (e.g., social interaction, speech, gastrointestinal measures, hyperactivity, toilet training, stereotypical movements, etc.) recited in the claims with notable improvements following treatment in several of these measures. Similarly, limitations reciting the assessment of fecal chymotrypsin levels prior to and after administration of the digestive enzymes (as in claims 58, 65, 77, 88, 92, 105, 115, 119, 131, 139, 152, 156 and 168) would be obvious to the skilled artisan to assess the efficacy of treatment, wherein based upon the successful increase in

pancreatic enzyme secretion following secretin administration taught by Beck, the skilled artisan would reasonably expect that chymotrysin levels would also be elevated following digestive enzyme therapy. One of ordinary skill in the art would also recognize that it is desirable to compare the chymotrypsin measurements in the autistic individuals to values obtained from age-matched non-autistic controls (i.e., a normal level) where appropriate, such as for initial assessment and comparison purposes as in claims 54, 82, 84, 109, 140, 141, and 148. Therefore, such claim limitations do not render the recited method of treatment non-obvious over the prior art.

With respect to the limitation "said amount is determined according to the age of the individual" in claims 56, 86, 111, 113, and 150, it is obvious to administer a dose in this manner as the dosage amount of virtually all medications are determined according to the age and/or weight of the individual being treated. With respect to the limitation of frequency of administering the enzyme in claims 57, 87, 113, 114, and 151, Sipos teaches that the total amount of the composition required to be administered to an enzyme deficient patient will vary with the severity of the condition and the amount of food ingested. Sipos notes, for instance, that for a pancreatic enzyme deficiency patient, the pancreatic enzyme composition is administered with each meal. Considering that the average person in a non-developing nation consumes an average of 3 meals a day and sometimes more (including snacks), administration of pancreatic enzymes would therefore encompass daily administration 3-6 times per day. And with respect to limitations reciting the duration of treatment (the digestive enzymes are administered over a period of 6 months, such as in claims 74, 102, 128 and 165), it is

noted that Beck teaches treatment and assessment of autistic individuals for several weeks to months. Because of the nature of autism, the skilled artisan would readily recognize that long-term therapy may be required to achieve beneficial therapeutic effects. Given the state of the art at the time the invention was filed, and the teachings of Sipos, determining the proper duration for administering digestive enzymes or a proper therapeutic regimen is well within the skilled artisan's purview, and it does not constitute novel inventive concept.

Regarding claim limitations reciting specific fecal chymotrypsin levels associated with autism, Bode reports chymotyrpsin levels for both normal (i.e., >10 U/gm; range 10 - 59.5 U/gm)) and pathological (4.2 U/gm; see 2.2 on p. 3334) values. As these disclosed levels and ranges encompass the presently recited values (i.e., a level below 8.4 U/gm; a level below 8.4 U/gm but above or equal to 4.2 U/gm; a level below 4.2 U/gm), and therefore could be used to determine pancreatic insufficiency in an individual consistent with the method of the present invention. Moreover, even though Bode teaches measurement of chymotrysin levels at 25°C instead of the claimed 30°C, this limitation is clearly a result effective protocol parameter that at a person of ordinary skill in the art would routinely optimize (see MPEP 2144.05). Optimization of parameters is a routine practice that would be obvious for a person of ordinary skill in the art to employ, particularly in a laboratory protocol. It would have been customary for an artisan of ordinary skill to determine the optimal temperature for measurement of chymotrypsin levels. Running the assay at a higher temperature would have been obvious, since it would run faster. One of ordinary skill in the art would have been

motivated to optimize this variable, and selection of a temperature well below body temperature (37 °C) would have been obvious. Thus, absent some demonstration of unexpected results from the claimed parameters, this optimization of temperature would have been obvious at the time of Applicants' invention.

Response to Arguments

12. In the response filed October 28, 2009, Applicant argues that none of the references, alone or in combination, teach or suggest the presently claimed method. Applicant asserts that Beck does not teach treating autistic individuals that have digestive enzyme deficiencies by first measuring the level of fecal chymotrypsin and then administering digestive enzymes to those with lowered fecal chymotrypsin levels, nor does Beck mention evaluating the levels of any hormones or enzymes in fecal matter. Applicant argues that Beck's subgrouping of autistic patient having "gastrointestinal symptoms" or "gastrointestinal abnormalities" are broad generic descriptions that can encompass many disorders, and do not provide the level of specificity regarding an expected reduced fecal chymotrypsin level or exocrine pancreatic insufficiency disorder to prompt a skileed artisan to modify Beck with the method of Bode and Sipos. Applicant further asserts the Beck in fact teaches away from evaluating chymotrypsin levels in fecal matter, as Beck suggests that such levels will be normal and will provide no useful information in the treatment of autistic patients, including, in particular, information regarding whether to administer digestive enzymes to autistic patients. In Applicant's view, Beck does not suggest that supplementation of

digestive enzymes of any type would provide any therapeutic value to an autistic patient, and instead only suggest the administration of secretin to such patients. Further, Applicant argues that neither Bode nor Sipos cure the deficiencies of Beck, as there is no motivation to use the teachings of either reference to modify the teachings of Beck. Finally, Applicant asserts that there would be no reasonable expectation of success that chymotrypsin levels, and particularly fecal cymotrypsin levels, could be a biomarker for the subsequent use of digestive enzymes to treat autistic patients.

Applicant's arguments filed October 28, 2009 have been fully considered but they are not persuasive. In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, the entirety of the Beck reference is directed to the treatment and evaluation of autistic patients, wherein the crux of the disclosed invention amelioration of gastrointestinal problems as a means to treat autism, such as by the administration of an agent (secretin) that induces the release of pancreatic digestive enzymes. This would suggest to the skilled artisan that correction of pancreatic digestive enzyme insufficiency is necessary for the effective treatment of autism, particularly in those individuals having gastrointestinal abnormalities. The skilled artisan would have also recognized that more

sensitive and more easily-administered diagnostic techniques, as opposed to the highly-invasive and time-consuming duodenal enzyme release assays described by Beck, would have been necessary in order to evaluate such digestive enzyme deficiencies. The teachings of Bode provide a simple, non-invasive, inexpensive and highly accurate means to assess pancreatic insufficiency in patients, by the measurement of fecal chymotrypsin levels. Hence, the skilled artisan would have had ample motivation to use such an assay to assess the pancreatic digestive enzyme status in autistic individuals, wherein such assessment would reasonably be expected to lead to the correlation of chymotrypsin levels with autistic status, such as for use as a diagnostic biomarker. As discussed above, it would obvious to use digestive enzyme levels, such as fecal chymotrypsin levels, as markers to either instigate treatment and/or to monitor treatment efficacy.

Moreover, the fact that the most positive effects on relieving autistic symptoms were demonstrated by Beck to have occurred in secretin-treated patients who had significantly increased pancreatic enzyme fluid secretion would have suggested to the skilled artisan that the administration of digestive enzymes themselves would be beneficial for the treatment of autism. Notably, Sipos teaches that compositions comprising digestive enzymes can be used to treat patients having exocrine pancreatic insufficiencies. As discussed above, the combined teachings of Beck and Sipos would have lead the ordinary-skilled artisan to reasonably predict that administration of oral digestive enzymes, which are far less invasive than the secretin infusions performed by Beck, would also be efficacious in improving autistic symptoms in patients.

Therefore, taken together the combined teachings of the above references still render obvious the presently recited invention.

Conclusion

13. Claims 51, 53-62, 64-75, 77, 81-90, 92-103, 105, 109-117, 119-129, 131, 135-154, 156-166 and 168-169 are rejected. Claims 76, 104, 130 and 167 are objected to and have not be further treated on the merits. Claims 63, 78-80, 91, 106-108, 118, 132-134, 155, and 170-171 are objected to as being dependent upon a rejected base claim, but would otherwise be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kimberly Ballard whose telephone number is 571-272-2150. The examiner can normally be reached on Monday-Friday 8:30 AM - 5 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Stucker can be reached on 571-272-0911. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Kimberly Ballard
Art Unit 1649

/Daniel E. Kolker/
Primary Examiner, Art Unit 1649
January 4, 2010